

Please amend the first full paragraph of page 4 of the specification as follows.

Attached is a marked up copy showing changes to the specification.

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Further embodiments of the present invention concern the subject matter of the further claims. Other features and advantages of the invention can be derived from the description of the preferred embodiments and figures. The sequence protocols and figures are now briefly described.

After the brief description of Figure 2 (first full paragraph) and before the second full paragraph at page 5 of the specification, please insert the following.

-- Figure 3 discloses a Western blot indicating the production of MP52 using vaccinia viruses as expression systems.

Figure 4 discloses a schematic view of the plasmid pABWN.

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Figure 5 discloses a section of an implant (matrix-bound MP52, 26 days after implantation) stained according to von Kossa. Mineralized tissue in black is clearly distinguished from the surrounding muscle tissue.

Figure 6 discloses a partial cross-section view of the implant of Figure 5, but stained according to Masson-Goldner.

Please amend the paragraph spanning pages 13 and 14 of the specification as follows. Attached is a marked up copy showing changes to the specification.

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The clone was completed up to the 3' end of the cDNA according to the method described in detail by Frohmann (Amplifications, published by Perkin-Elmer Corp., Issue

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5 (1990), pp 11-15). The same embryonic mRNA that had been used to isolate the first fragment of MP-52 was reversally transcribed as described above. The amplification was carried out using the adapter primer (AGAATTCGCATGCCATGGTTCGACG) (SEQ ID NO:3) of the MP-52 sequence. The amplification products were reamplified using an overlapping adapter primer (ATTCGCATGCCATGGTTCGACGAAG) (SEQ ID NO:5) and an overlapping internal primer (GGAGCCCACGAATCATGCAGTCA) (SEQ ID NO:6) of the MP-52 sequence. After restriction cleavage with NcoI the reamplification products were cloned and sequenced into a vector that was cleaved in the same way (pUC 19 (Pharmacia No. 27-4951-01) having a modified multiple cloning site which contains a single NcoI restriction site) and sequenced. The clones were characterized by their sequence overlapping at the 3' end of the known MP-52 sequence. One of these was used as a probe to screen a human genomic gene bank (Stratagene No. 946203) according to a method described in detail by Ausubel et al. (Current Protocols in Molecular Biology, published by Greene Publishing Associates and Wiley-Interscience (1989)). One phage (λ 2.7.4) was isolated from 8×10^5 λ phages which contained an insertion of about 20 kb and which is deposited at the DSM under the depository number 7387. This clone contains further sequence information at the 5' end in addition to the sequence isolated from mRNA by the described amplification methods.

Please amend the paragraph spanning pages 14 and 15 of the specification as follows. Attached is a marked up copy showing changes to the specification.

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The genomic DNA contains an intron of about 2 kb between base paris 1270 and 1271 of SEQ ID NO:1. The sequence of the intron is not shown. The correctness of the

splicing site was confirmed by sequencing an amplification product which was derived from cDNA containing this region. These sequence informations were obtained using a slightly modified method which is described in detail by Frohmann (Amplifications, published by Perkin-Elmer Corporation, Issue 5 (1990), pp 11-15). The same embryonic RNA that was also used to isolate the 3' end of MP-52 was reverse transcribed using an internal primer orientated in the 5' direction of the MP-52 sequence (ACAGCAGGTGGGTGGTGTGGACT) (SEQ ID NO:7). A polyA tail was attached to the 5' end of the first cDNA strand using terminal transferase. A two-step amplification was carried out, firstly by using a primer composed of oligo dT and an adapter sequence (AGAATTCGCATGCCATGGTTCGACGAAGC(T16)) (SEQ ID NO:8) and secondly an adapter primer (AGAATTCGCATGCCATGGTTCGACG) (SEQ ID NO:3) and an internal primer (CCAGCAGCCCATCCTTCTCC) (SEQ ID NO:9) from the MP-52 sequence. The amplification products were reamplified using the same adapter primer and an overlapping internal primer (TCCAGGGCACTAATGTCAAACACG) (SEQ ID NO:10) from the MP-52 sequence. Subsequently the reamplification products were reamplified using an overlapping adapter primer (ATTCGCATGCCATGGTTCGACGAAG) (SEQ ID NO:5) and an overlapping internal primer (ACTAATGTCAAACACGTACCTCTG) (SEQ ID NO:11) from the MP-52 sequence. The final reamplification products were cloned with blunt ends into a vector (Bluescript SK, Stratagene No. 212206) which had been cleaved with EcoRV. The clones were characterized by their sequence overlapping with the DNA of λ 2.7.4.

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Please amend the paragraph spanning pages 21 and 22 of the specification as follows. Attached is a marked up copy showing changes to the specification.

For this the HindIII fragment from plasmid pSK52s that starts with nucleotide 576 in SEQ ID NO. 1, was isolated and the protruding ends were made blunt by treatment with Klenow fragment. A Not I restriction cleavage site was introduced at both ends of the fragment by ligation of the adapter.

Adapter: AGCGGCCGCT (SEQ ID NO:12)

TCGCCGGCGA (SEQ ID NO: 41)

C¹² Vector pABWN was restricted with XhoI, also treated with the Klenow fragment and dephosphorylated with intestinal alkaline phosphatase from the calf (Boehringer Mannheim). The same phosphorylated adapter was ligated on so that an insertion of the MP52 fragment after restriction with NotI into the generated Not I cleavage site of the vector was now possible. The expression vector that results is subsequently denoted HindIII-MP52/pABWN. All the reactions carried out for the cloning were carried out according to standard methods (e.g. CP units 3.16).

IN THE SEQUENCE LISTING:

Please delete pages 36-52 containing the Sequence Listing and insert new pages 36-52 containing the revised Sequence Listing.

REMARKS